

## WHAT IS CLAIMED IS:

1. A method of producing a virus, comprising:
  - a) inoculating and culturing host cells in an appropriate medium at a  
5 temperature below a physiological optimum for host cell growth;
  - b) infecting the host cells with a virus, resulting in virus-infected host cells;
  - c) culturing the virus-infected host cells at or near a physiologically optimum  
temperature for producing virus;
  - d) harvesting virus and/or cells containing virus from the culture; and,
  - 10 e) purifying virus away from host cell and culture contaminants, resulting in a  
purified virus product.
2. A method of producing a virus, comprising:
  - a) inoculating and culturing host cells in an appropriate medium at a  
15 temperature at or near a physiological optimum for host cell growth;
  - b) shifting the temperature of the host cell culture of step a) to a temperature  
below a physiological optimum for host cell growth;
  - c) infecting the host cells of step b) with a virus, resulting in virus-infected  
host cells;
  - 20 d) culturing the virus-infected host cells at or near a physiologically optimum  
temperature for producing virus;
  - e) harvesting virus and/or cells containing virus from the culture; and,
  - f) purifying virus away from host cell and culture contaminants, resulting in a  
purified virus product.
- 25 3. A method of according to claim 2 wherein the culture temperature is  
lowered to a sub-optimal level for at least about 24 hours prior to infecting the host  
cells with the virus.
- 30 4. A method according to claim 2 wherein the culture temperature is  
lowered to a sub-optimal level for up to the entire cell passages prior to infecting the  
host cells with the virus.

5. A method of producing adenovirus, comprising:
- a) culturing host cells at a temperature below a physiological optimum for promoting host cell growth;
  - b) infecting the host cells with an adenovirus, resulting in adenovirus-infected host cells;
  - c) culturing the adenovirus-infected host cells at or near a physiologically optimum temperature for producing adenovirus;
  - d) harvesting virus and/or cells containing virus from the culture; and,
  - e) purifying virus away from host cell and culture contaminants, resulting in a purified virus product.
6. A method of producing adenovirus, comprising:
- a) inoculating and culturing host cells in an appropriate medium at a temperature at or near a physiological optimum for host cell growth;
  - b) shifting the temperature of the host cell culture of step a) to a temperature below a physiological optimum for host cell growth;
  - c) infecting the host cells of step b) with a adenovirus, resulting in adenovirus-infected host cells;
  - d) culturing the adenovirus-infected host cells at or near a physiologically optimum temperature for producing adenovirus;
  - d) harvesting virus and/or cells containing virus from the culture; and,
  - e) purifying virus away from host cell and culture contaminants, resulting in a purified virus product.
7. A method according to claim 6 wherein the culture temperature in step b) is lowered to a temperature below a physiological optimum for up to the entire cell passages prior to infecting the host cells with the adenovirus.
8. A method according to claim 6 wherein the culture temperature in step b) is lowered to a temperature below a physiological optimum for at least 24 hours prior to infecting the host cells with the adenovirus.
9. A method according to claim 6 wherein the temperature for cell growth in step b) is from between 31°C and 34°C.

10. A method according to claim 7 wherein the temperature for cell growth in step b) is from between 31°C and 34°C.

5 11. A method according to claim 8 wherein the temperature for cell growth in step b) is from between 31°C and 34°C.

10 12. A method according to claim 7 wherein the temperature for cell growth in step a) is from between 35°C and 38°C and the temperature for cell growth in step b) is from between 31°C and 34°C.

13. A method according to claim 8 wherein the temperature for cell growth in step a) is from between 35°C and 38°C and the temperature for cell growth in step b) is from between 31°C and 34°C.

15 14. A method according to claim 7 wherein the temperature for cell growth in step a) is from between 35°C and 38°C and the temperature for cell growth in step b) is from between 31°C and 34°C and the temperature for growth of infected host cells of step c) is from about 36°C and 38°C.

20 15. A method according to claim 8 wherein the temperature for cell growth in step a) is from between 35°C and 38°C and the temperature for cell growth in step b) is from between 31°C and 34°C and the temperature for growth of infected host cells of step c) is from about 35°C and 38°C.

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